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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/879,320	06/12/2001	Ajay Hasmukhlal Upadhyay	RD 01022	5176

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EXAMINER	
CHANNAVAJJALA, LAKSHMI SARADA	
ART UNIT	**PAPER NUMBER**
1615	

DATE MAILED: 06/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/879,320	UPADHYAY, AJAY HASMUKHLAL	
	Examiner	Art Unit	
	Lakshmi S Channavajjala	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 February 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6-10 and 30-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-4, 6-10 &30-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt of amendment dated 2-17-04 is acknowledged.

Claims 5 and 32 have been canceled. Claims 1-4, 6-10 and 30-38 are pending.

The following rejection of paper # 11 has been maintained:

Claim Rejections - 35 USC § 103

Claims 5-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over 4,711,774 to Denick, Jr. et al (Denick).

Claim 5 has been canceled and claim 1 has been amended by instant amendment. Accordingly, the above rejection is applied to claims 1, and 6-8.

Denick, teaches a particulate composition comprising guaifenesin and magnesium aluminum silicate. Denick teaches that the particle size of the composition, upon milling to a free flowing composition, is about 100 microns (example 1). Further, Denick suggests that the particulate size ranging from 10 to 150 microns is suitable for the invention i.e., to prepare a guaifenesin composition containing magnesium aluminum silicate as an adsorbate. As explained above, instant claims do not specify any binder and accordingly, magnesium aluminum silicate of Denick reads on instant binder. Denick differs from the instant claims in the percentages of particle sizes. Instant Claim 5 requires 10-60 percent particles in the range of 45 to 150 microns; claim 6 requires > 10% particles having > 75 microns and > 55% particles having 45 microns; claim 7 requires < 25% exhibit a size range greater than 425 microns, 17%-55% particles are in a range of 45-150 microns and > 85% particles have > greater than 45 microns. It would been obvious for one of an ordinary skill in the art at the time of the instant invention to choose and

obtain guaifenesin composition having claimed particle sizes because Denick teaches that suitable particle sizes in the range of 10-150 microns are preferred for adsorbing sufficient quantities of medicament solution to prepare an acceptable drug product.

Denick does not state the flow rate recited in claim 8. However, it is the position of the examiner that because Denick teaches particles in the same size range as required by the claims, optimizing the flow rate to produce a free flowing particulate formulation, having the claimed flow rate would have been obvious for a skilled artisan at the time of the instant invention.

Claims 1-10 and 30-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,372,252 to Blume et al (hereafter Blume) in view of US 4,269,859 to Morse.

Instant amendment canceled claims 5 and 32. Accordingly, the instant rejection is applied to claims 1-4, 6-10, 30, 31 and 33-38.

Blume teaches sustained release formulations comprising guaifenesin, a hydrophilic polymer such as hydroxypropyl methylcellulose, a water insoluble polymer and other tabletting ingredients (col. 4, lines 4-28 and col. 6, lines 1-43). Among the pharmaceutical additives, Blume teaches lubricants such as magnesium stearate, calcium stearate etc; binders such as povidone (polyvinylpyrrolidone), gelatin, starch; glidants such as talc or silicon dioxide, stabilizers and other excipients such as lactose, sorbitol etc (col. 6, lines 45-65). Further, Blume teaches preparing the composition by granulation and compression (col. 8), which includes as one of the steps, drying and milling the composition and passing through sieves of 100 mesh screen size (col. 8, lines 20-25). Examiner notes that a 100-mesh size screen allows for particles

of 150-micron size (see instant description on page 14). Blume does not teach the exact percentages of the particle sizes as claimed.

Morse teaches a method of tabletting using cellulosic floc granules, which acts as a binder and a disintegrant, and which imparts good flow and binding characteristics. Morse teaches making tablets by direct compression involves three requisites: free-flowing particulate material, binding properties of the material and material that does not stick to punches or dies (col. 1). Further, Morse teaches that the cellulosic binding material should have an average particle size in the range of 20 and 55 microns or even 30 to 40 microns (col. 2 and col. 7). Further, Morse teaches that cellulose particles of the above size range impart a good flow properties (example 13) and adequate tablet hardness, binding strength and stability due to the flow rate and the binding properties for binding the tablet to itself (Col.8). Morse further suggests admixing the cellulosic floc with other pharmaceutical excipients such as starch, lactose, dextrose, mannitol, carboxymethyl cellulose; lubricants such as magnesium stearate, PEG and other excipients such as talc, silica, dicalcium phosphate (col. 8, lines 45-67), which are also described in the instant specification. Further, Morse also suggests that the amount of excipient, lubricant or binder should not be employed at such levels as to reduce the necessary and desirable free-flow characteristics of the cellulose granules themselves (col. 9). Accordingly, it would have been obvious for one of an ordinary skill in the art at the time of the instant invention to use the appropriate particle sizes binders, disintegrants and such tabletting aids in the guaifenesin containing composition of Blume because Morse teaches that free-flowing characteristics in a compressible tablet preparation is a function of particle size and that the free-flowing binder material (with a particle size of 30 to 55 microns) imparts the desired hardness,

strength and stability to the tablet. Further, optimizing the amounts of binders, lubricants and other excipients in the guaifenesin comprising medicament formulation of Blume would have been within the scope of a skilled artisan because Morse suggests that the amounts o excipients should such that the flow characteristics should not be affected.

Response to Arguments

Applicant's arguments filed 2-17-04 have been fully considered but they are not persuasive.

Denick 103(a):

Applicants state that instant claim 1 has been amended to include guaifenesin particles and binder, which is now applicable to claims 6-8. Applicants argue that Denick does not disclose any composition that comprises guaifenesin particles. Applicants also argue that instant invention would not have been obvious to one of an ordinary skill in the art at the time the instant invention was made, from the teachings of Denick because Denick's disclosure of a mixture of a liquid solution of guaifenesin and magnesium alumina silicate particles for sorbing the dissolved guaifenesin would not suggest instant claimed particle of guaifenesin and a binder. However, applicants' attention is directed to example 1 (col. 11, lines 33-43) where guaifenesin solution is mixed with magnesium aluminum silicate to forma homogenous mass and the dried mass is milled to produce free flowing particulate material having a particle size of 100 microns. Thus, the resulting particulate material of Denick contains particles of both guaifenesin and magnesium aluminum silicate and not just magnesium aluminum silicate particles as argued by applicants. Further, Denick clearly teaches the desire to produce a free flowing particulate composition comprising guaifenesin. Accordingly, it would have been obvious for one of an

ordinary skill in the art to produce a particulate guaifenesin composition with a desired particle size and an optimum flow rate of the particles.

Blume in view of Morse 103(a):

Applicants argue that Blume teaches a directly compressible guaifenesin granulation comprising 95% guaifenesin and 5% binder that is made by granulating, milling and screening a mixture of guaifenesin and a binder. Further, it is argued that at least 60% of Blume's granulation has a particle size of greater than 150 microns and less than 200 microns. While it is agreed by the examiner that Blume does not teach the exact claimed percentages of particles, the particle sizes taught by Blume is well within the claimed range. Instant claims state that greater than 80% of the particles have a size above 45 microns and less than 30% have a size of greater 425 microns. In other words, a majority of the particles have a size range between 45 microns and 425 microns. Thus, even according to applicants' interpretation of the teachings of Blume i.e., 60% of particles in the size range of 150 nm to 200 nm, instant particle sizes are encompassed by the particle sizes taught by Blume.

Applicants argue that Morse does not disclose guaifenesin composition having the claimed particle size distribution and instead teaches cellulose granules wherein the cellulose fibers having an average length on their longest dimension of 20 to 50 microns. Applicants also argue that Morse recognizes that the flow rate of a particulate mixture of cellulose granules is impacted by various components of the mixture, their amounts and the size of the particles i.e., addition of certain excipients reduce the desirable flow properties. Applicants further argue that the flow properties of mixtures of cellulose granules become unpredictable (as taught by Morse) and hence instant invention would not have been obvious to one of an ordinary skill in the art.

However, applicants' arguments are not persuasive because data provided in the instant specification indeed proves the teachings of Morse that free-flowing characteristics in a compressible tablet preparation is a function of particle size and that the free-flowing material having the claimed particle size imparts the desired hardness, strength and stability to the tablet in terms of friability, capping, moisture etc (data on pages 22-27 of the instant application). Besides, as admitted by applicants, Morse also suggests that the desired flow properties can be achieved using an appropriate binder or other excipients, and by adjusting the levels of excipients. In the instant specification it is noted that applicants employ only maltodextin and PVP as the excipients in all of the inventive examples, where it has not been explained what or if the comparative examples contain any excipients. Further, applicants also did not compare the flow properties, friability, moisture content of instant composition with different binders or other excipients. Accordingly, in the absence of any comparison between binders, instant unexpected results can only be attributed the specific binders tested and one of an ordinary skill in the art would expect (from Morse disclosure) that the claimed properties are indeed a function of several factors including the particle size and the excipients such as binders, as well as their levels. Therefore, for the reasons the rejection has been maintained.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

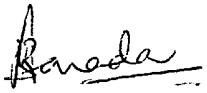
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lakshmi S Channavajjala whose telephone number is 571-272-0591. The examiner can normally be reached on 7.30 AM -4.00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on 571-272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Lakshmi S Channavajjala
Examiner
Art Unit 1615
June 4, 2004